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PARATHYROID HORMONE RECEPTOR LIGANDS

Cross-Reference to Related Applications

[0001] This application is a continuation of international application number PCT/US00/16776 filed June 15, 2000, and claims the benefit of priority of international application number PCT/US00/16776 having international filing date of June 15, 2000, designating the United States of America and published in English, which claims the benefit of priority of U.S. provisional patent application no. 60/139,335, filed June 15, 1999; both of which are hereby expressly incorporated by reference in their entireties.

Field of the Invention

[0002] The present invention relates to ligands of PTH2 and PTH1 receptors, wherein said ligands may be peptides, fragments and analogs thereof having PTH2 or PTH1 receptor binding activity, and methods for using same.

Background of the Invention

Parathyroid hormone receptors

[0003] The parathyroid hormone receptors (PTH receptors) are part of an extended family of receptors. Usdin, *et al.*, *J Biol Chem* 270:15455-15458 (1995). The human parathyroid hormone type 2 receptor (PTH2 receptor) shares about 51% amino-acid sequence identity with the human parathyroid hormone type 1 receptor (PTH1 receptor). Both PTH receptors belong to the Type II family of G-protein-coupled receptors which respond to peptide modulators, including calcitonin, glucagon, secretin and vasoactive intestinal polypeptide. Both PTH receptors are activated by PTH, but only the PTH1 receptor is activated by parathyroid hormone-related protein (PTHrP). The PTH2 and PTH1 receptors, together with their ligands, have presumably evolved to selectively mediate different physiological functions.

Parathyroid hormone 2 receptor

[0004] The PTH2 receptor is a G-protein coupled receptor selectively activated by parathyroid hormone (PTH) and not by PTHrP. The first demonstration of this was by Usdin *et al.* (*J Biol Chem* 270:15455-15458 (1995)) and later by Behar *et al.* (*Endocrinology* 137:2748-57 (1996)) and Gardella *et al.* (*J Biol Chem* 271:19888-19893 (1996)). It is most